

DOCKET NO.: CHIR-0158 (0316.005)
PATENT APPLICATION

SERIAL NO.: 09/360,934
FILED: JULY 26, 1999

At line 4 of the insert, insert --now abandoned,-- after "October 21, 1994,".

01
At page 4, line 1, after "and host cells." insert --The present invention provides cytotoxin polypeptides that exhibit substantially no toxicity, or substantially reduced toxicity. The present invention also provides CAI and heat shock polypeptides that exhibit no functional contribution to toxicity, or a substantially reduced functional contribution to toxicity.--

At page 53, line 8, after "EFKNGKNKDFSK" insert --(SEQ ID NO:9)--.

At page 53, line 8, after "EPYIA" insert --(SEQ ID NO:10)--.

At page 60, line 22, delete "thenpresent" and insert --the presence--.

At page 60, line 23, delete "pylor" and insert --pylori--.

Please insert the enclosed sheet entitled "Abstract" after the claims.

Please append to the end of the specification the enclosed substitute Sequence Listing (pages 1 - 19).

IN THE CLAIMS:

Please cancel, without prejudice, claims 41, 44, and 47 in the original application, amend claims 38 - 40, 42, 43, 45, 46, and 48 - 50, and add new claims 51 and 52 as follows.

02
Claim 38 (Amended). A ~~[purified protein of the]~~ recombinantly produced *Helicobacter pylori* cytotoxin (CT) polypeptide, wherein the recombinantly produced polypeptide exhibits substantially no toxicity, or substantially reduced toxicity.

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Claim 39 (Amended). [The purified protein of claim 38 wherein said protein is] A recombinantly produced fragment of a *Helicobacter pylori* CT polypeptide, wherein the recombinantly produced fragment (i) comprises at least about ten amino acids, (ii) can induce the production of antibodies to *Helicobacter pylori*, and (iii) exhibits substantially no toxicity, or substantially reduced toxicity.

C2
sub
D1
cont

Claim 40 (Amended). A [polypeptide sequence of the *Helicobacter pylori* cytotoxin amino acid sequence set forth in] recombinantly produced *H. pylori* CT polypeptide or fragment thereof comprising SEQ ID NO:3 or a fragment thereof, which polypeptide [sequence] or fragment thereof : (i) comprises at least [five] about ten amino acids of SEQ ID NO:3, (ii) can induce the production of antibodies to *Helicobacter pylori*, and (iii) exhibits substantially no [contribution to] toxicity, or substantially reduced toxicity.

Claim 42 (Amended). The polypeptide [sequence] of claim 40, wherein said [sequence] polypeptide comprises [about five to] at least about fifteen amino acids.

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D2

Claim 43 (Amended). A prophylactic or therapeutic vaccine comprising an immunologically effective amount of a *H. pylori* CT polypeptide [sequence of the *Helicobacter pylori* cytotoxin amino acid sequence set forth in] comprising SEQ ID NO:3 or a fragment thereof, which polypeptide [sequence]: (i) comprises at least [five] about ten amino acids of SEQ ID NO:3, (ii) can induce the production of antibodies to *Helicobacter pylori*, and (iii) exhibits substantially no [contribution to] toxicity, or substantially reduced toxicity.

Claim 45 (Amended). The vaccine of claim 43, wherein said [sequence] polypeptide comprises [about five to] at least about fifteen amino acids.

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Claim 46 (Amended). The vaccine of claim 43, [which] further [comprises] comprising an immunologically effective amount of a second polypeptide [sequence of the *Helicobacter*] comprising *H. pylori* cytotoxin associated immunodominant (CAI) antigen or a fragment thereof, which second polypeptide [sequence]:

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(i) comprises at least [five] about ten amino acids, (ii) can induce the production of antibodies to *Helicobacter pylori*, and (iii) exhibits [substantially] no functional contribution to toxicity, or a substantially reduced functional contribution to toxicity.

Claim 48 (Amended). The vaccine of claim 46, wherein said [sequence] second polypeptide comprises [about five to] at least about fifteen amino acids.

Claim 49 (Amended). A method of [preparation of] preparing a prophylactic or therapeutic vaccine [which comprises] comprising bringing into association:

- (1) an immunologically effective amount of a [polypeptide sequence of the *Helicobacter pylori* cytotoxin] H. pylori CT polypeptide, which polypeptide [sequence]: (i) comprises at least [five] about ten amino acids, (ii) can induce the production of antibodies to *Helicobacter pylori*, and (iii) exhibits substantially no [contribution to] toxicity, or substantially reduced toxicity, and
- (2) a pharmaceutically acceptable carrier.

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Claim 50 (Amended). The method of claim 49, [which] further [comprises] comprising adding an immunologically effective amount of a second polypeptide [sequence of the *Helicobacter*] comprising H. pylori [cytotoxin associated immunodominant (CAID)] antigen or fragment thereof [amino acid sequence set forth in SEQ ID NO:5], which second polypeptide [sequence]: (i) comprises at least [five] about ten amino acids, (ii) can induce the production of antibodies to *Helicobacter pylori*, and (iii) exhibits [substantially] no functional